



Management of Adult Male Hypogonadism

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Outline

- Definition
- Prevalence
- Causes
- Types
- Clinical Features
- Investigation and Diagnosis
- Treatment
- Follow up
- Summary
- References



Definition and prevalence

- Male hypogonadism is a condition in which the body doesn't produce enough of the hormone that plays a key role in masculine growth and development during puberty (testosterone) or enough sperm or both
- Prevalence is estimated at between 2.1% (middle aged) and 38.7% (elderly men). Yeo et al. In people with diabetes its 40-90% (Musa et al, Olopade et al)

Gross and
Microscopic
Structure of
the testes



Anatomy of male urogenital system

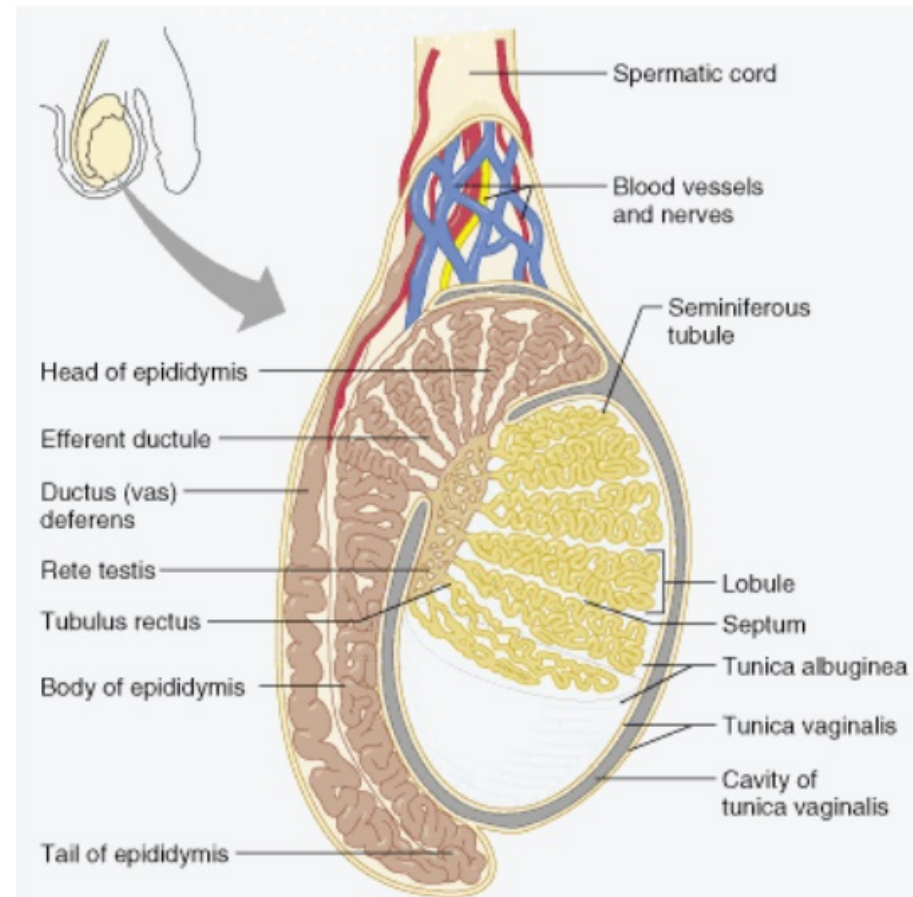
- Males have 2 testes which work with the UGT



Anatomy of the testes

- Spermatic cord
- Epididymis
- Vas deferens
- Seminiferous tubules

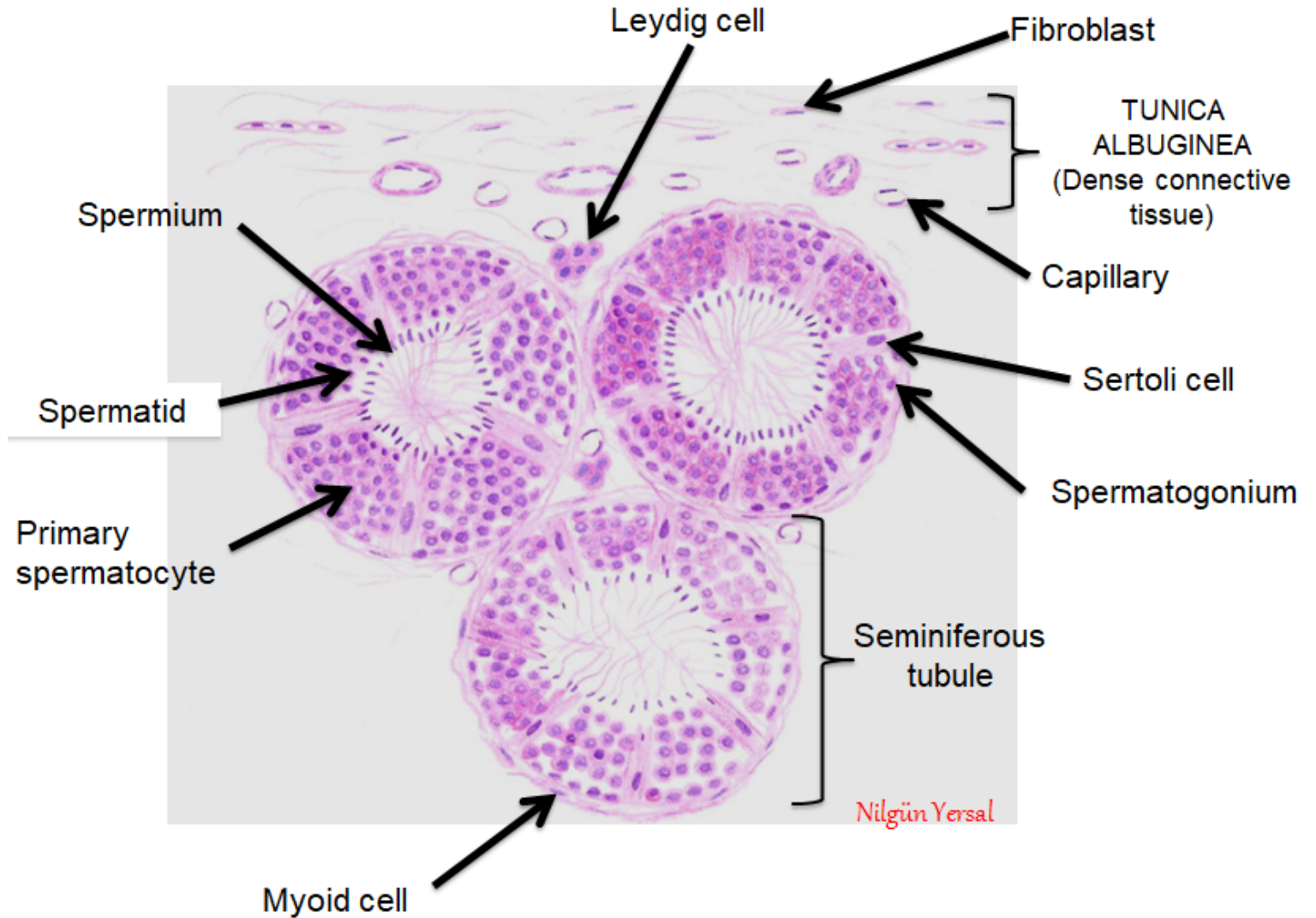
Histology of testis



(a)

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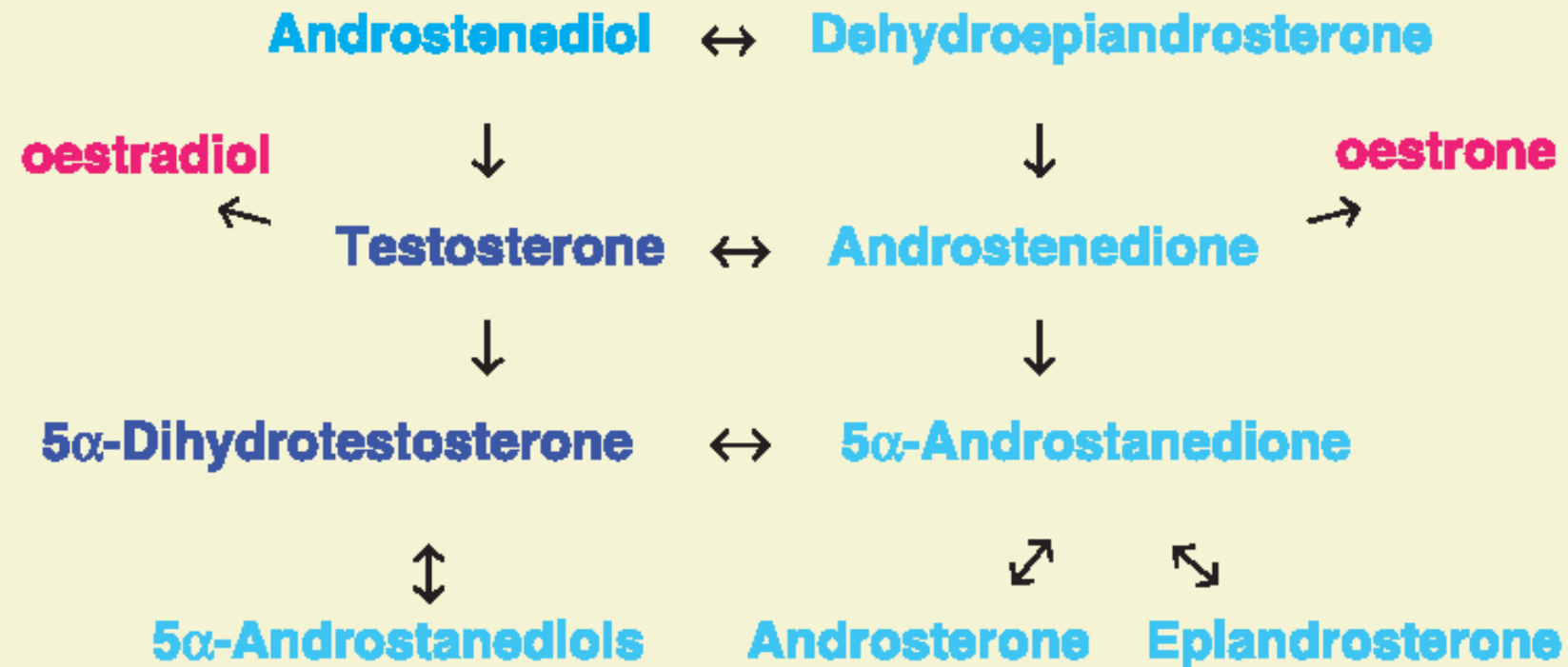
Leydig cells, tubules, Sertoli cells



Physiology

- Testosterone is produced by the testes, it is bound by the SHBG in circulation and the levels regulated by FSH and LH
- Testosterone levels drop 1% yearly after age 30. By 50 years of 20% of men have hypogonadism, by 60yrs 30% and by 70 yrs 50% have hypogonadism
- It induces the onset of male puberty and increases the features of masculinity such as facial hair, increased muscle mass and bone mass

Androgen metabolism



CLASSIFICATION or TYPES

- **Hypergonadotrophic**

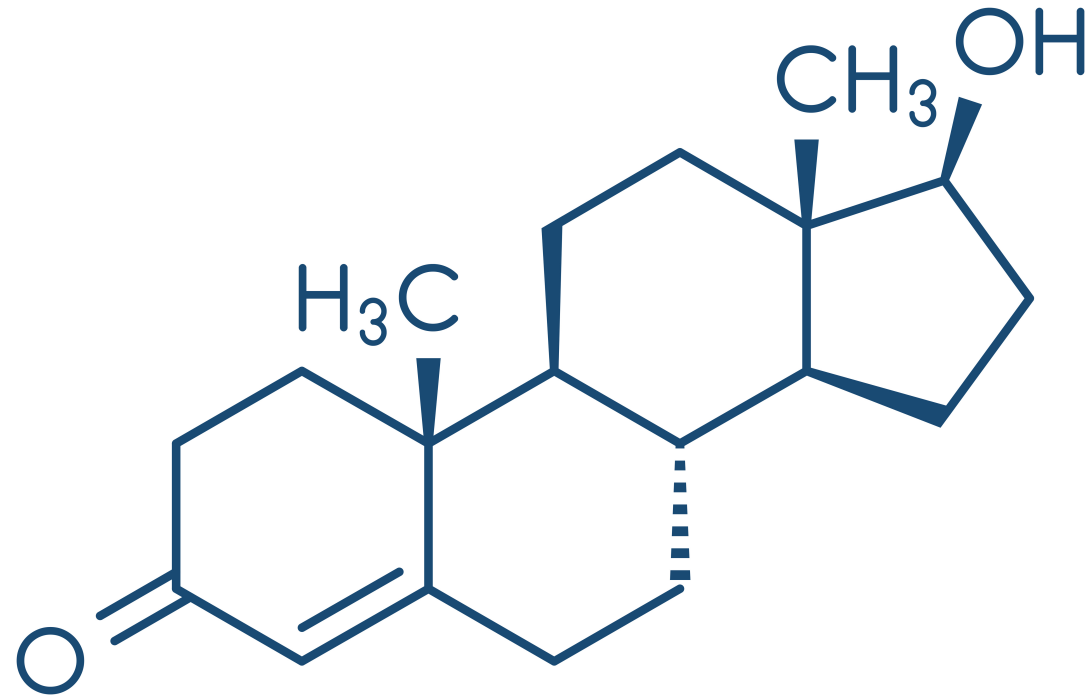
- Klinefelters syndrome
- Chemotherapy and radiation therapy
- Gonadectomy
- Anorchism and cryptorchidism
- Sertoli only cell syndrome (del Castillo syndrome)

- **Hypogonadotrophic**

- Kallman's syndrome
- Prader-Wili syndrome, Laurence – Moon Biedl syndrome, Bardet-Biedl syndrome
- Gaucher's disease
- HIV/AIDS, Cushing's syndrome, obesity, T2DM

Biochemistry

- This is a hormone of androstane class
- Produced by testicular Leydig cells
- Binds to the SHBG
- Deactivated to DHT and estradiol
- It is responsible for testicular descent, puberty related secondary sexual characteristics
- Measured between 8-10am

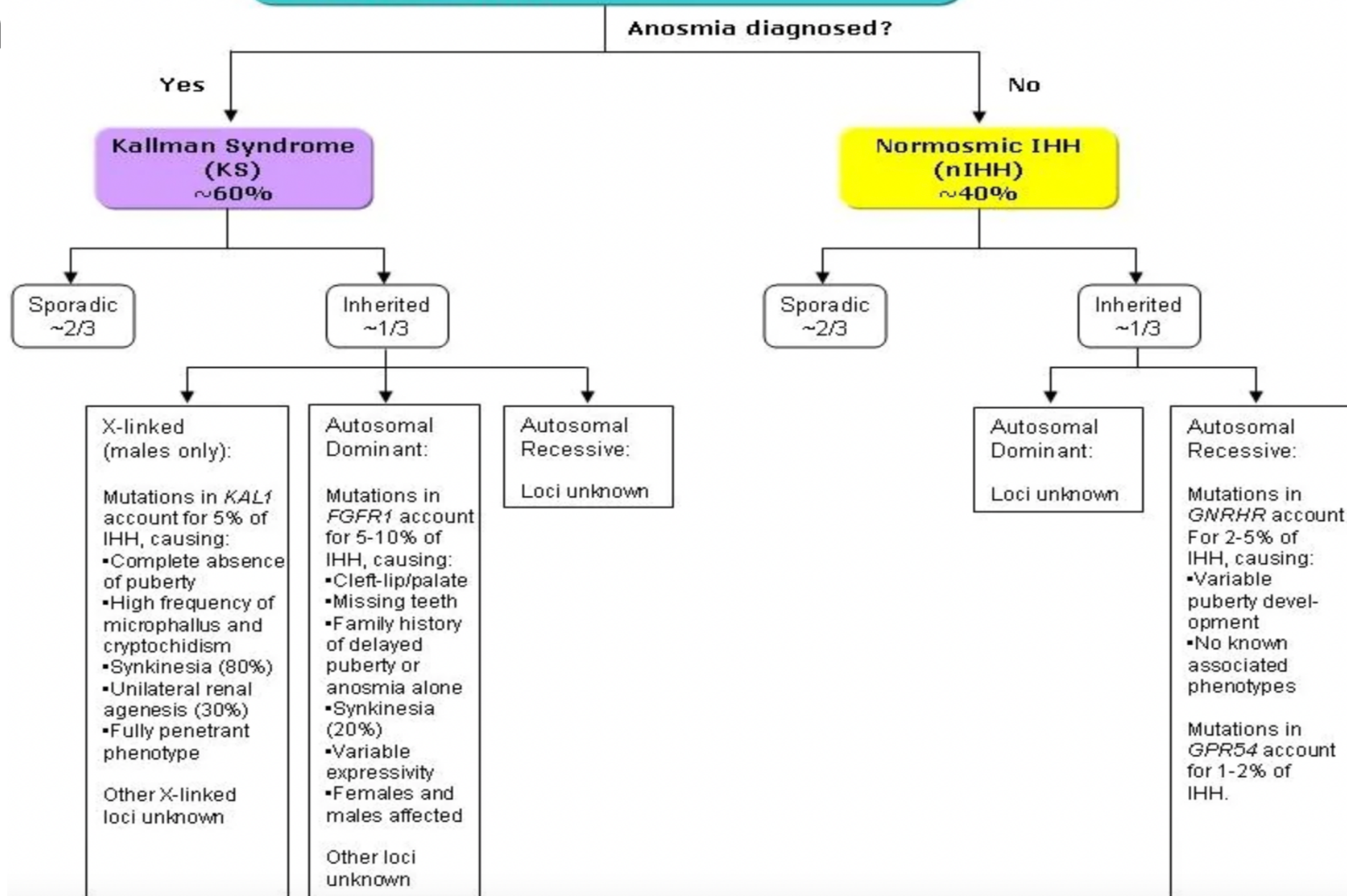


testosterone

Androgen - Pharmacokinetics

- Absorption: undergoes high first pass metabolism. Therefore IM injections or synthetic preparations are used
- Transport: highly protein bound in plasma to albumin & sex hormone binding globulin (SHBG) (98%, SHBG, albumin)
- Metabolism:
 - by liver enzymes : androsterone & etiocholanolone
 - excretion by urine after conjugation
 - small quantity of oestrogen also produced from testosterone, but not from fluoxymesterone and Dihydrotestosterone

- Absent or incomplete puberty
- Low or normal LH/FSH in the context of low T or E₂
- Normal pituitary function/MRI
- Normal ferritin levels



Causes of Primary Hypogonadism

A) Congenital

- Chromosomal defect e.g Klinefelter's syndrome
- Congenital anorchia
- Androgen receptor/ enzyme defect

B) Acquired

- Testicular trauma or injury
- Surgical removal
- Chemotherapy/ Irradiation
- Infections e.g Mumps Orchitis

C) Complication of illness e.g: Diabetes, renal failure, cirrhosis.

Clinical Features of Male Hypogonadism

These are sexual and non sexual related

Clinical Features of Adult male hypogonadism

- Low libido
- Poor morning erections
- Erectile dysfunction
- Depressed mood
- Fatigue
- Decreased vitality
- Cognitive impairment
- Insulin resistance
- Obesity, abdominal obesity
- Metabolic syndrome
- Arterial hypertension
- Diabetes mellitus type 2
- Decreased muscle mass and strength
- Decreased bone mineral density and osteoporosis
- Use of glucocorticoids, opioids, antipsychotics

Objective evaluation through questionnaires

- ADAM (Androgen deficiency in Aging Males) Questionnaire
- AMS (Aging Male Symptom) scale
- MMAS (Massachussets Male Aging Study) questionnaire

Table 3. Signs and Symptoms of Hypogonadism

Signs of Hypogonadism

Incomplete sexual development
Gynecomastia
Loss of axillary and pubic hair
Small or shrinking testes
Infertility related to low sperm counts
Height, BMD, and muscle loss
Anemia, mild (normochromic, normocytic)
Increased BMI and body fat percentage

Symptoms of Hypogonadism

Reduced libido and activity
Decreased spontaneous erections
Hot flashes
Fatigue, decreased motivation
Depression or dysthymia
Poor concentration and memory
Sleep disturbance or increased sleepiness

BMD, bone mineral density; BMI, body mass index.

Investigations

Evaluation of erectile dysfunction patient

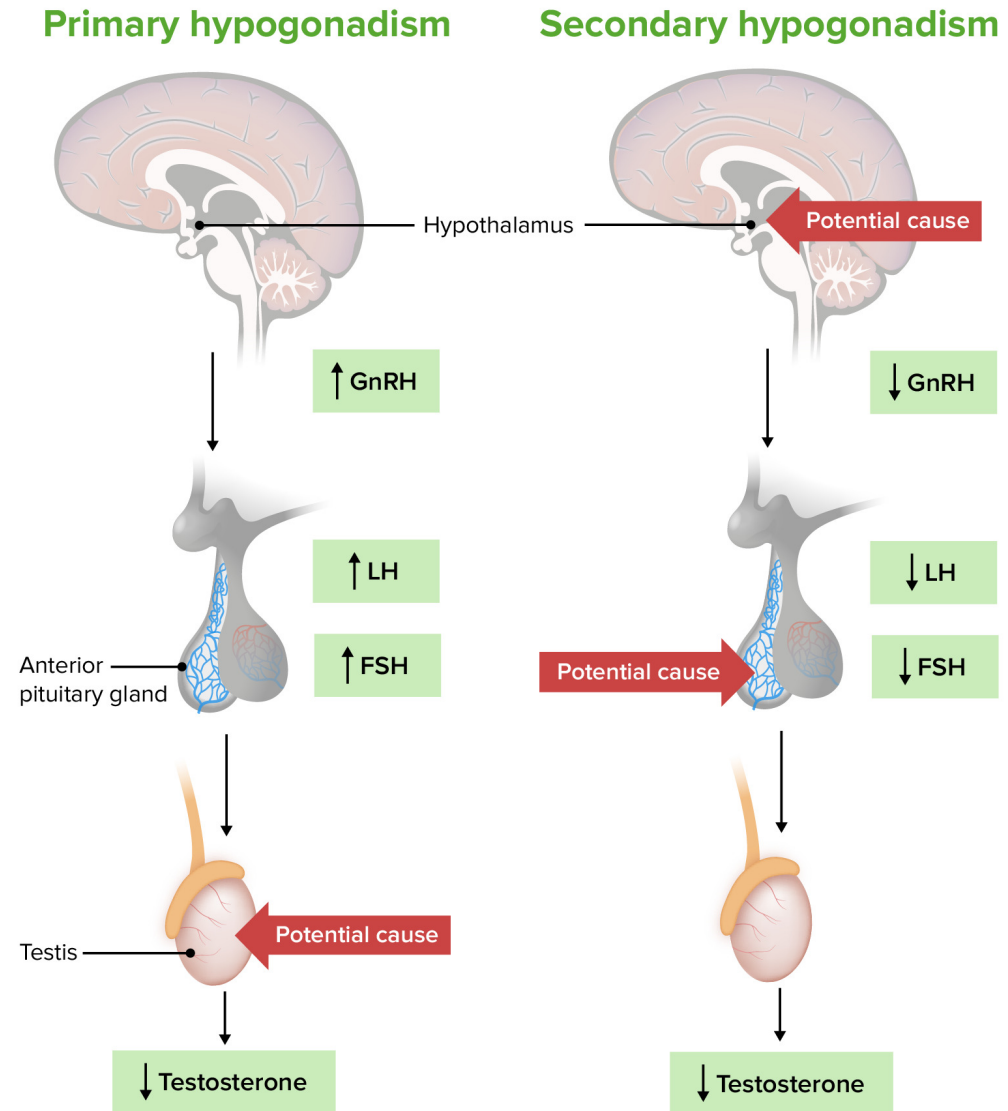
- Ask patient or partner
- Visual analogue scales
- Questionnaires
- Bulbocavernous reflex
- Postage stamp tests
- Penile blood pressure
- Penile biothesiometry
- Cavernosometry
- Penile doppler scan
- Hormone profiles
- MRI magnetic resonance angiography

Not all erectile dysfunction is due to hypogonadism

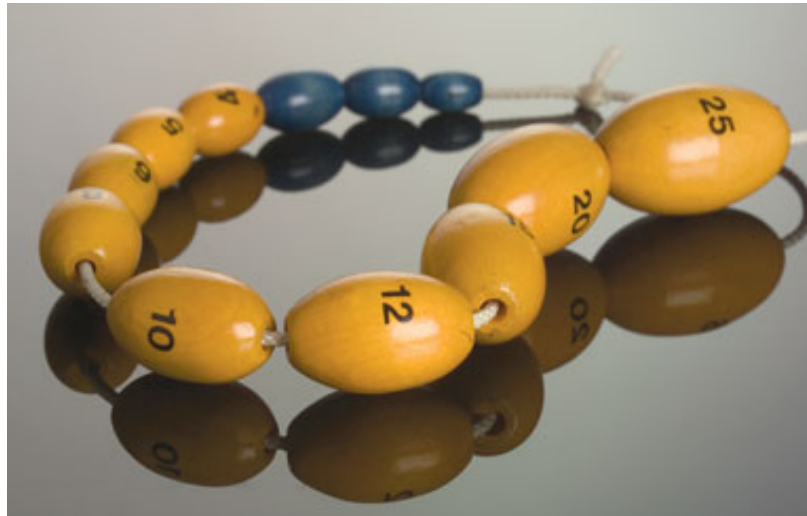
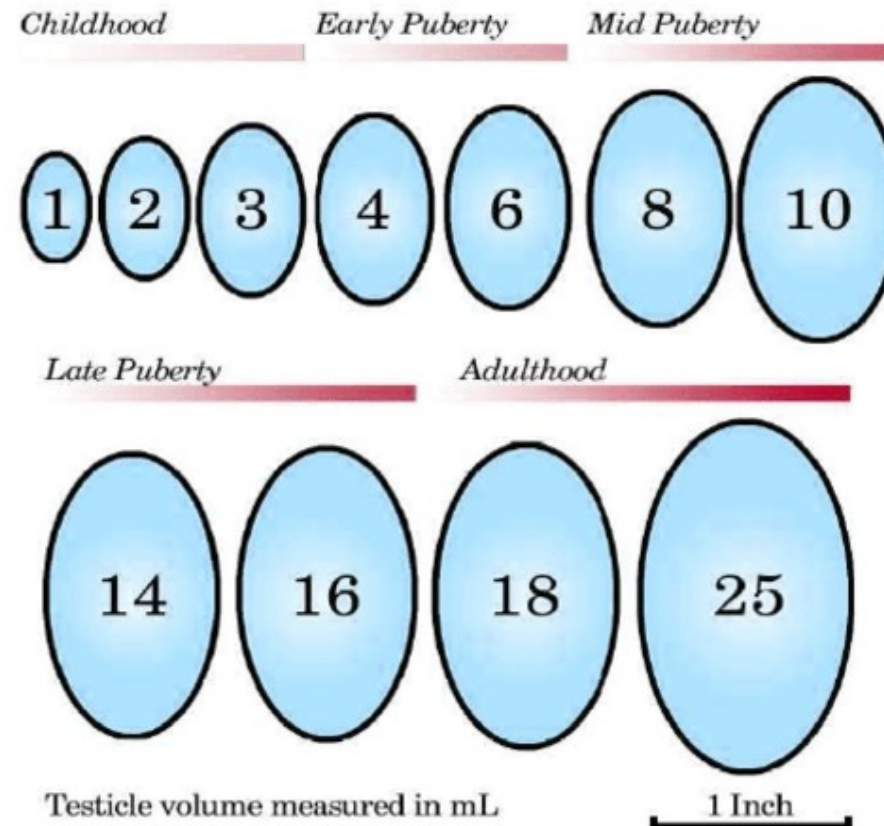
- Cavernosal disease
- Diabetes mellitus
- Aging
- Neurologic disorders
- Kidney disease
- Drugs
- Surgery
- Psychological
- Lifestyle
- Hypogonadism

Primary/ Secondary hypogonadism

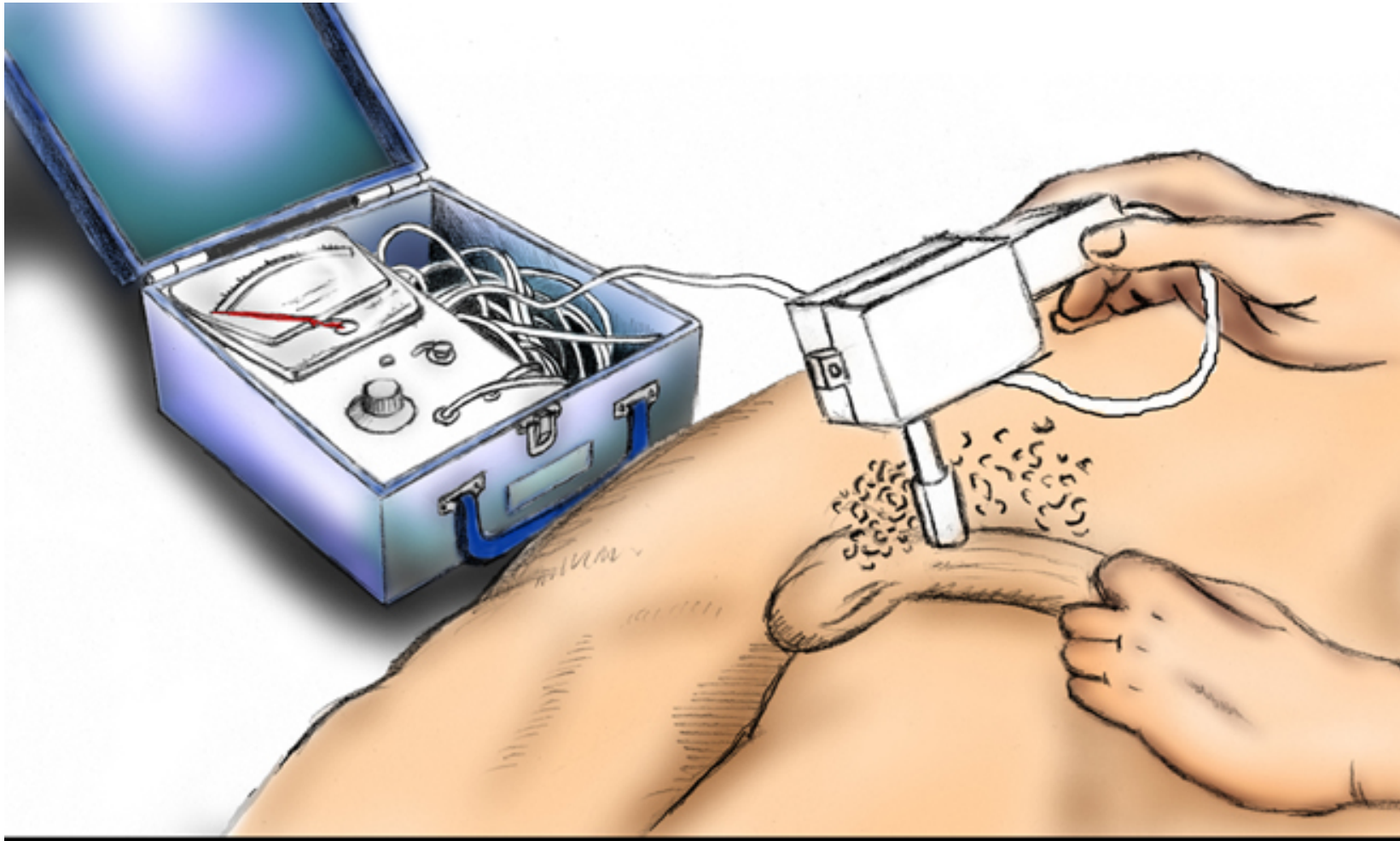
- Primary causes are in testes and secondary are in the hypothalamus/pituitary axis



Orchidometer

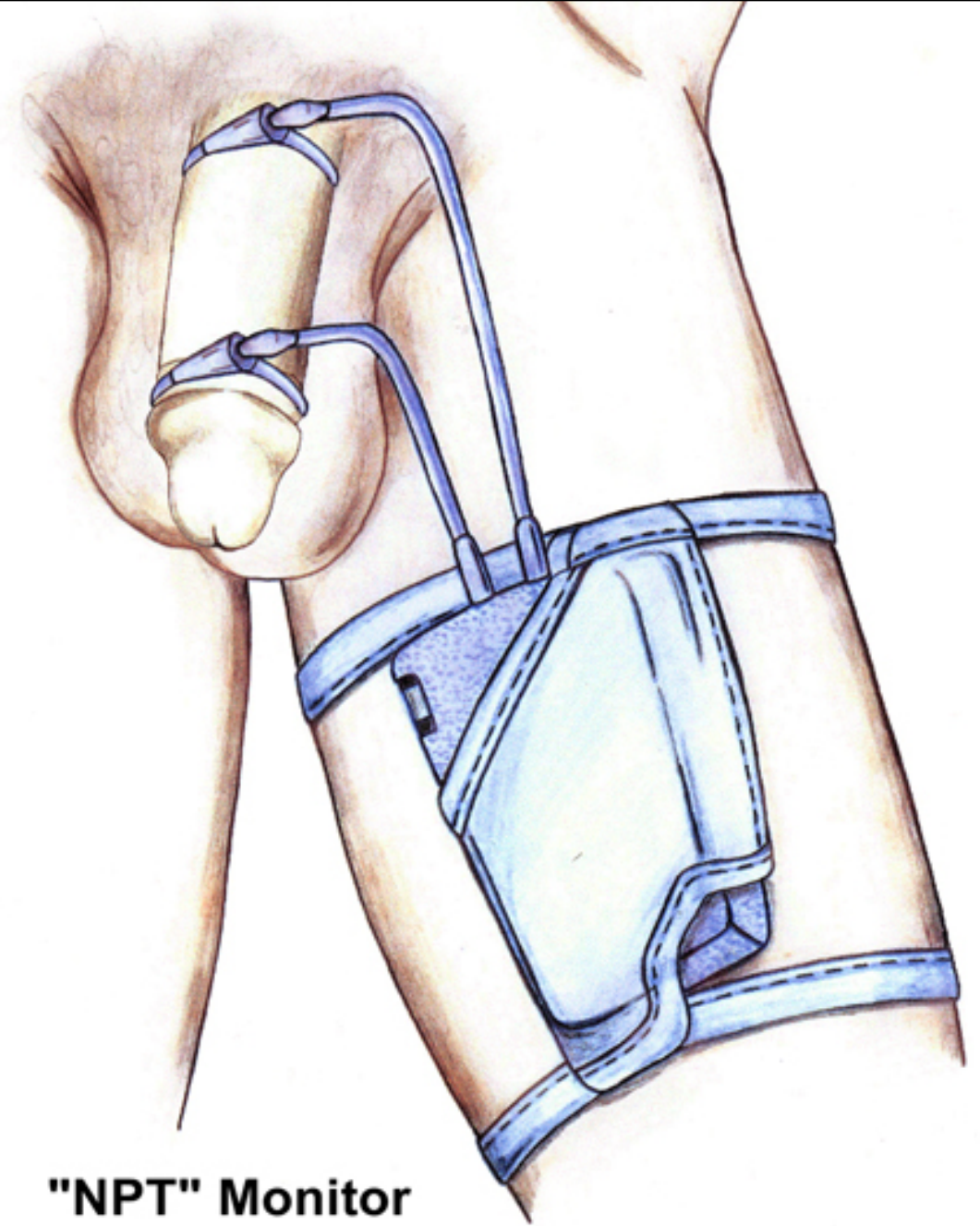


Biothesiometry

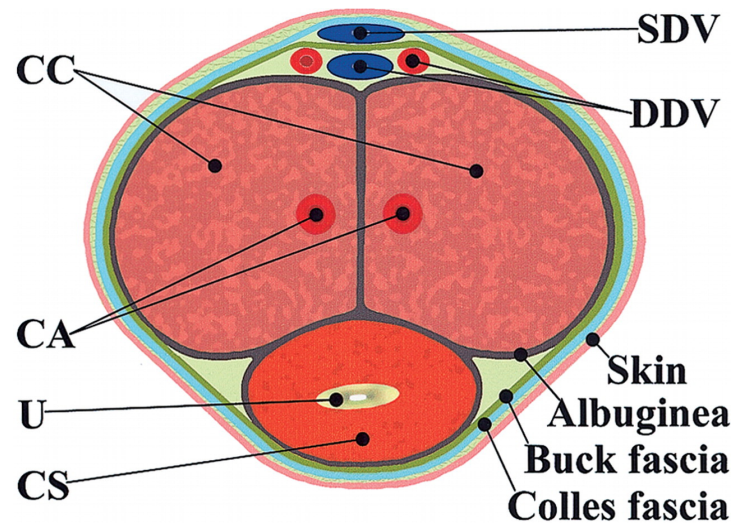


Skin Vibration Testing (Biothesiometry)

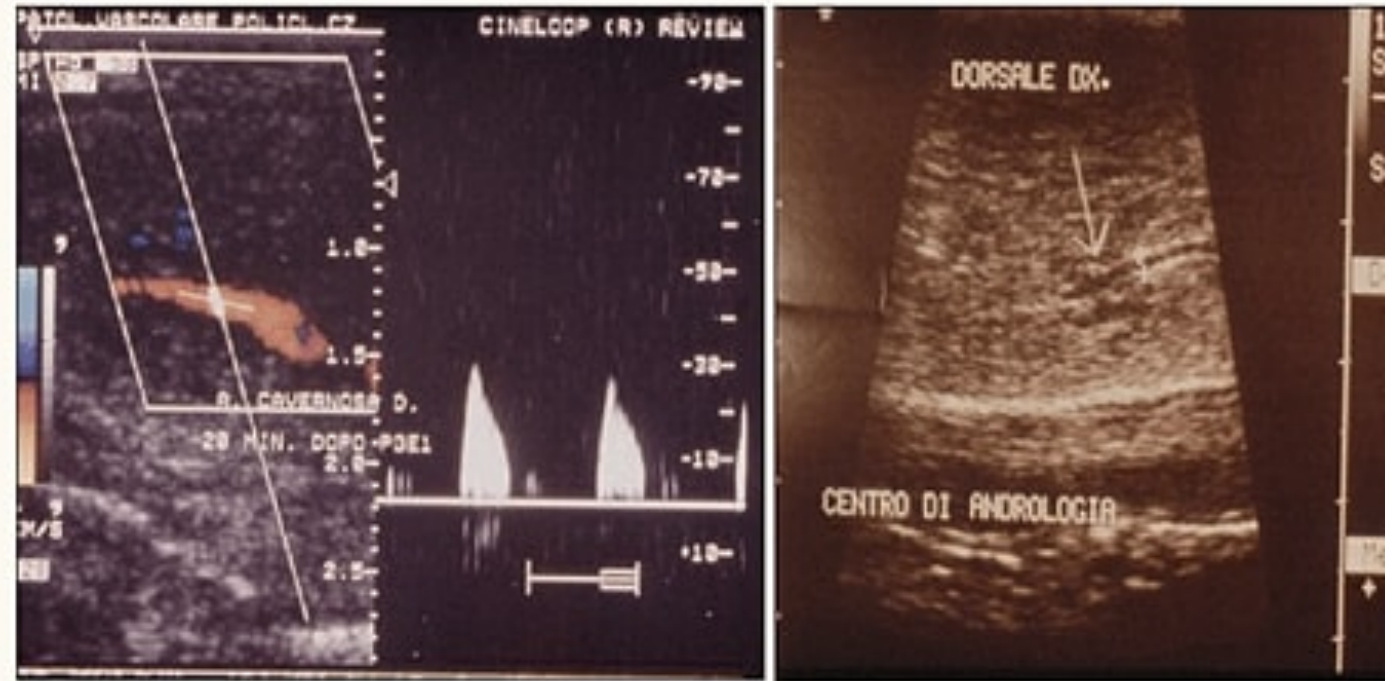
Evaluation of ED



"NPT" Monitor



Dynamic Penile Doppler Sonography



Courtesy of Vincenzo Mirone, MD.

Hormone assays

- Testosterone
- FSH
- LH
- Prolactin
- Estradiol
- Others

Testing for Testosterone

- Total testosterone (measures free T and that bound to proteins)
- Free testosterone (measures only active T)
- Bioavailable testosterone (free T plus that bound to albumin)
- *Testosterone is best tested between 8-10am when levels are highest*

Other hormone tests

FSH

LH

Oestradiol

Prolactin

PSA

TESTOSTERONE REPLACEMENT THERAPY



EAU Guidelines on Male Hypogonadism

Recommendation	LE	GR
The two forms of hypogonadism have to be differentiated, as this has implications for patient evaluation and treatment and makes it possible to identify patients with associated health problems and infertility.	1b	B

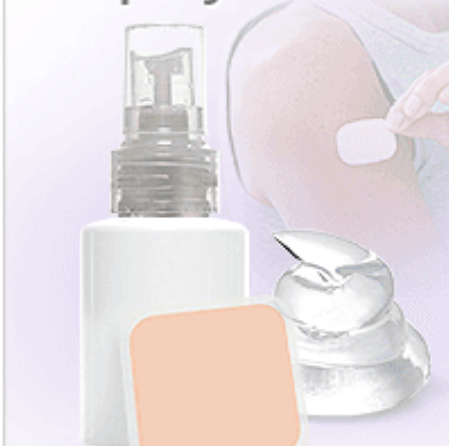
Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes:

An Endocrine Society Clinical Practice Guideline

“We recommend measurement of serum LH and FSH levels to distinguish between primary (testicular) and secondary (pituitary-hypothalamic) hypogonadism.”

Types of Testosterone Replacement Therapy

Testosterone replacement therapy is categorized according to its various routes of administration.

Oral	Sublingual	Transdermal	Intramuscular	Subcutaneous
• Pills 	• Drops 	• Creams • Patches • Gels • Sprays 	• Injections 	• Pellets 

Why we replace testosterone

- Metabolic
- Neurologic
- Genital/sexual
- Cardiovascular
- Musculoskeletal

The Benefits of TRT*

*Testosterone Replacement Therapy

BEFORE:

- Constant fatigue
- Depressed
- Increased fat tissue
- Increased risk of ED and low libido
- Increased risk of osteoporosis
- Increased risk of Alzheimer's Disease

AFTER:

- Increased muscle mass
- Sharper mind
- Confident
- Healthy heart
- Strong erections and healthy libido
- Strong bones
- High energy

OMC
Oregon Man Clinics

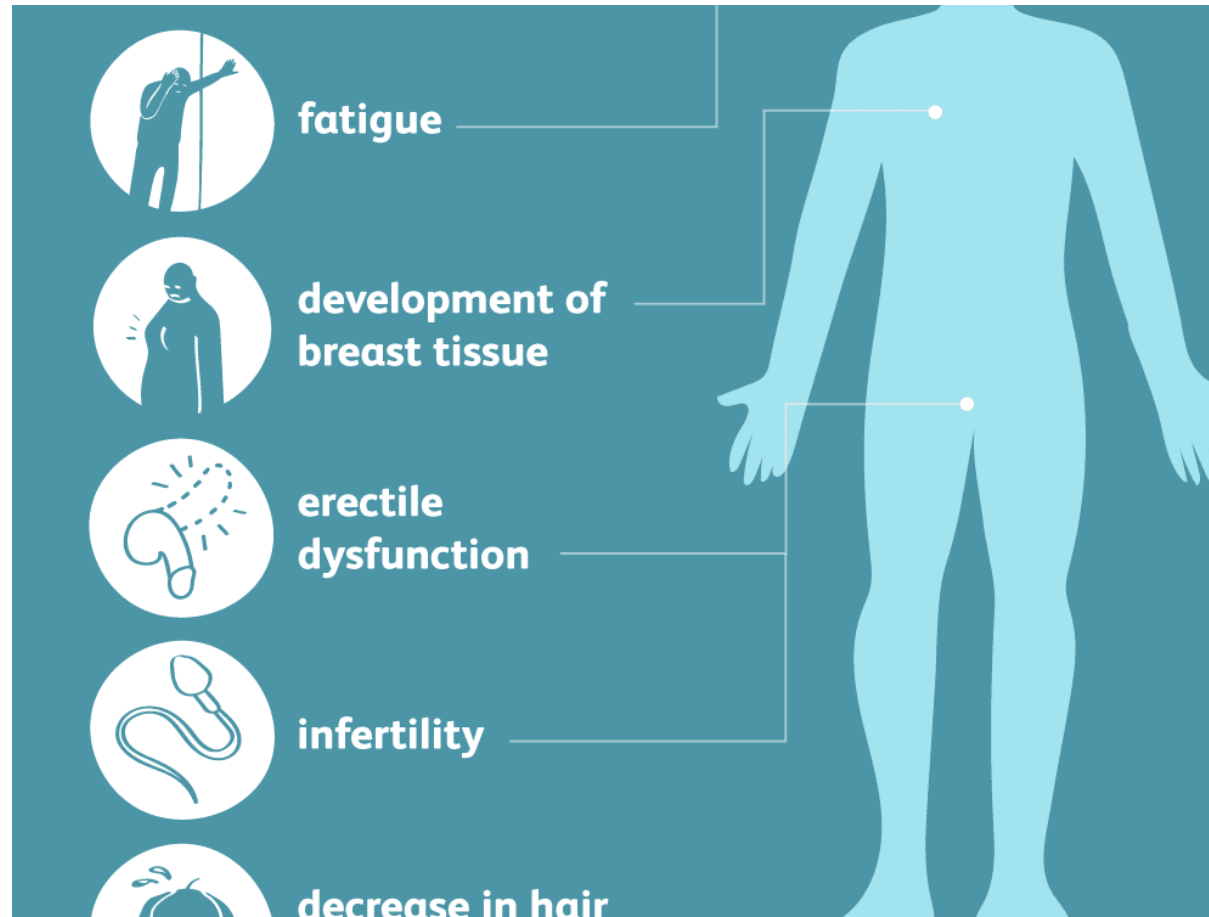
Eugene, Oregon | 541.505.8773 oregonmanclinics.com Bend, Oregon | 541.508.4858

Effects of testosterone replacement

- Libido and drive (vigor) are first features to improve
- Metabolic and musculoskeletal features improve after few months



Effects of Low Testosterone



Improving Libido and Erection

- Lifestyle, diet
- Exercise, weight training
- Testosterone
- PDE5 inhibitors like tadalafil and sildenafil
- In adolescent boys, it leads to development of sexual secondary characteristics



Male secondary sexual characteristics

External genitalia

- ❑ Penis increases in size
- ❑ Scrotum becomes pigmented and rugose

Internal genitalia

- ❑ Seminal vesicles enlarge.
- ❑ Prostate and seminal vesicles enlarge

Voice

- ❑ Larynx enlarges, vocal cords increase in length and thickness – voice becomes deeper

Hair Growth

- ❑ Beard appears. Hairline to scalp recedes.
- ❑ Pubic hair grows with male pattern
- ❑ Hair in axilla, on chest and around anus

Mental

- ❑ More aggressive
- ❑ Active attitude
- ❑ Interested in opposite sex

Body conformation

- ❑ Broad shoulders
- ❑ Enlarging muscles

Skin

- ❑ Sebaceous gland secretion thickens and increases (predisposing to acne)



Restoring or Preserving Fertility

- A major drawback of testosterone replacement is the reduction in sperm count
- Those still desirous of having children require weekly or twice weekly dose of hCG, usually 2,500iu twice weekly
- Testicular Sperm extraction (TESE) and storage should be considered
- Lifestyle, antioxidants and other supplements

Testosterone formulations

	Route	Frequency	
Testosterone cypionate	Injection	2-3 weekly	
Testosterone enanthate	Injection	2-3 weekly	
Testosterone undecanoate	Injection	Quarterly	
Testim	Dermal	daily	
Androgel	Dermal	Daily	
Andriol	Oral	Daily	
Pellets/patches	Dermal/transdermal	3-6 monthly for pellets	

Monitoring Men Receiving Testosterone Therapy

- ❑ Evaluate the patient **3 to 6 months** after treatment initiation and then **annually** to assess whether symptoms have responded to treatment and whether the patient is suffering from any adverse effects.
- ❑ Monitor **testosterone level 3 - 6 months** after initiation of testosterone therapy:
- ❑ Therapy is aimed to raise serum testosterone level into the mid-normal range.
- ❑ **1) Injectable testosterone enanthate or cypionate:** *measure serum testosterone level midway between injections. If testosterone is 700 ng/dl (24.5 nmol/liter) or 400 ng/dl (14.1 nmol/liter), adjust dose or frequency.*
- ❑ **2) Transdermal patches:** *assess testosterone level 3–12 h after application of the patch; adjust dose to achieve testosterone level in the mid-normal range.*
- ❑ **3) Buccal testosterone bio-adhesive tablet:** *assess level immediately before or after application of fresh system.*

Adverse effects of testosterone replacement

- Increased prostate size (up to 12%)
- Anecdotal reports of increased cancer of prostate risk
- Polycythemia,
- Fluid retention, may cause cardiovascular problems
- Gynaecomastia/breast pain
- Worsening of obstructive sleep apnea

Androgen abuse

REPRODUCTIVE SYSTEMS

Female

Irregular menstrual cycle;
Clitoral hypertrophy;
Uterine and breast atrophy;
cervical and/or
endometrial cancer.

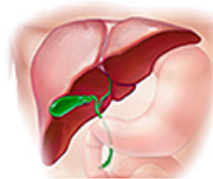


Male

Decreased endogenous
androgens production;
testicular atrophy;
infertility;
prostatic hypertrophy;
prostate cancer.



LIVER



Hepatocellular damage;
cholestasis peliosis;
hepatic adenoma;
hepatocarcinoma;
increased cholesterol;
decreased HDL cholesterol.

CARDIOVASCULAR SYSTEMS



Hypertension thrombosis;
pro atherogenic effects;
left ventricular hypertrophy ;
Sudden Cardiac Death

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ENDOCRINE SYSTEMS

Decreased glucose.

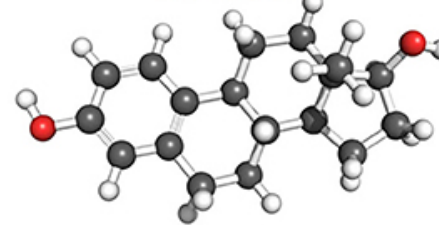


NEUROPSYCHIATRIC/BEHAVIORAL INVOLVEMENT

Mood swings;
aggressive behavior;
depression;
psychosis;
addiction withdrawal and
dependency disorders.

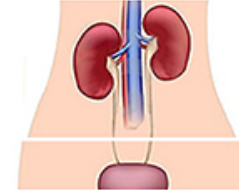


ADVERSE AASs EFFECTS



URINARY

Creatinine acute renal failure;
focal segmental glomerulosclerosis;
membranoproliferative glomerulonephritis.



INTEGUMENT

Acne, alopecia,
hirsutism,
male pattern baldness,
edema.



MUSCULOSKELETAL

Early epiphyseal closure in adolescents;
increased rate of muscle strains/ruptures;
increased risk of musculoskeletal



LARYNX

Deepening of the voice.



Contraindications to testosterone therapy

- Prostate nodule
- Breast cancer
- Prostate cancer
- Those with heart failure or COPD
- Those with high risk for thrombosis

Non-Testosterone based treatment

- **SERMs** : Clomiphene and tamoxifen
- **Aromatase inhibitors** : Anastrozole and letrozole
- **DHEAs** : Especially in men with adrenal insufficiency and hypogonadism

Summary

- Adult male hypogonadism is a condition which is commoner as males move from middle age to elderly age groups
- It could be hypergonadotrophic or hypogonadotrophic
- There are diverse causes to this condition and only thorough hx, exam can identify the causes
- Treatment often involves testosterone replacement or other non testosterone based treatments
- Testosterone replacement corrects most of the sex related, metabolic and musculoskeletal deficiencies associated with hypogonadism

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Appreciation

- We thank you all for your attention and participation



Dear God,
Thank you for
everything